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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/778,548 | 02/07/2001 | David M. Lubman | UM-06102 | 5017 |

23535 7590 01/27/2005
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EXAMINER

MARSCHEL, ARDIN H

ART UNIT PAPER NUMBER

1631

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/778,548

Applicant(s)

LUBMAN ET AL.

Examiner

Ardin Marschel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35,39-44,48,50,55-58,71,73-77,80-87 and 91 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 33,35,39,48,50,73-77,80-82 and 91 is/are allowed.
- 6) ☒ Claim(s) 1-8,17,18,21-25,58 and 87 is/are rejected.
- 7) ☒ Claim(s) 19,20 and 71 is/are objected to.
- 8) ☒ Claim(s) 1-35,39-44,48,50,55-58,71,73-77,80-87, & 91 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date (<u>1 sheet</u>). | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 10/4/04, have been fully considered and they are deemed to be persuasive regarding previous rejections/objections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. As, however, necessitated by amendments which have overcome previous rejections/objections and also which required the withdrawal of the specie election requirement as described below, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

As a result of the amendments, filed 10/4/04, the specie election requirement directed to the election of Specie A or B, in the election requirement, mailed 9/11/03, regarding whether there is a requirement for direct feeding of an output of a previous separating apparatus (e.g. HPLC) into a mass spectrometry apparatus or not is hereby withdrawn. The second specie election requirement in the election requirement, mailed 9/11/03 and modified in via the Exr. Int. Sum. of 10/2/03, regarding species C or D, directed to embodiments requiring a display of a first and/or second physical property regarding protein separation separate from mass spectrometry analysis or not, is maintained. Applicants have elected specie D directed to the no requirement for display election as set forth in said specie D description.

As a result of the above specie A/B election requirement withdrawal the following instant claims are presently under examination: Claims 1-8, 17-25, 33, 35, 39, 48, 50,

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58, 71, 73-77, 80-82, 87, and 91. Claims 9-16, 26-32, 34, 40-44, 55-57, and 83-86 are withdrawn as being directed to a non-elected specie.

VAGUENESS AND INDEFINITENESS

Claims 6-8, 21-25, and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 87 depends from cancelled claim 72 and therefore is vague and indefinite as to what limitations are meant therein. Clarification via clearer claim wording is requested.

Claims 6-8, 21, 24, and claims dependent therefrom, which contain abbreviations such as HPLC, ESI, oa, TOF, etc. are vague and indefinite as to what is specifically meant thereby due to such abbreviations unless replaced with their full names or the full names in parentheses therewith. Clarification via clearer claim wording is requested.

PRIOR ART

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, 17, 18, 21, 22, 25, 58, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (P/N 6,358,692).

Jindal et al. discloses the automated (instant claim 58) continuous multi-dimensional selection and analysis of molecules in the title and abstract as is the subject matter of the instantly claimed invention. Various separatory techniques; based on ligand physical properties; including ligand binding columns utilizing in a multi-dimensional system (column 3, line 35, through column 4, line 10); reverse phase columns involving partitioning, ion exchange, and pH separation (column 4, lines 23-40, and column 16, line 20, for reverse phase HPLC as in instant claim 6 and non-porous options thereof as in column 16, lines 64-67, as in instant claims 7, 21, and 22); mass spectrometry (column 4, line 17); size exclusion (column 3, line 29); liquid chromatograph (column 4, lines 41-55); and fluid velocity separation (column 5, lines 15-32) are described in the SUMMARY OF THE INVENTION section in columns 2-6. Charge based separation methods are those cited above as ion exchange or pH separation as also required for instant claim 3. The liquid phase separation of instant claim 5 are those such as in the above reverse phrase column methods, ion exchange, fluid velocity, etc. Thus, a variety of separation methodologies are summarized regarding separation of ligands. Ligands, thus separated, include proteins and other biopolymers, as indicated in column 5, lines 35-45, column 6, lines 3-14, and column 6, lines 54-58. Therefore, protein separation as instantly claimed is a clearly set forth suggested and motivated specie of ligand for practice in the instant invention. A library

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of proteins are thus provided, albeit digested, as cited in column 5, lines 35-45, of the reference as required in instant claim 1, line 3. Such a library being derived from a cell lysate sample as in instant claim 2 is set forth in Jindal et al. in column 8, lines 23-30. The column separation practice of tandem or multiple column steps is described in column 14, lines 40-56, which suggests and motivates first and second separating apparatus practices as in instant claim 1, lines 4-7 and parts b) and c). The direct feeding of previously separated protein ligands into a mass spectrometer as in instant claim 1, step d) with subsequent analysis and detection (instant claim 25) as in step e) is set forth in the reference in column 16, lines 18-32, as suggested and motivated by citing the system practice therein as being in an integrated system. Such integration is reasonably interpreted as being a direct feeding of sample from one stage to another in the stages of such a system. This citation additionally suggests and motivates the addition of any suitable dimension to the system. Jindal et al. also describes the practice whereby only a portion of the output of each separatory technique is carried on to the next separatory step as instantly claimed in instant claim 1, lines 11 and 15, for example, in column 3, line 44 ("subset of the column volumes"); column 3, line 58 (at least two subsets); column 4, line 14 (at least a portion); and column 4, lines 44-55 (sampler...to take a sample of the LC analysis peak"). The buffer system utilized in these carried forward samples are reasonably interpreted as being compatible from one separatory step to another due to both a lack of indication of a buffer change between stages as well a lack of limitation in instant claims 17, 18, and 87, for example, wherein compatibility is not limited to whether or not a buffer change may be utilized between

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steps. That is, in the practice of claims 17, 18, and 87 the buffer may be changed or not and still be compatible with first and second separating apparatus since there is no limitation in claims 17, 18, or 87 as to whether the buffer which is compatible must be present during actual separation practice or could be merely present at the start or end of a step and changed if desired.

Thus, it would be obvious to someone of ordinary skill in the art at the time of the instant invention to practice species of ligand including protein ligands in multi-dimensional, that is, multi-stage separatory methods, including direct feeding into mass spectrometry separation and analysis as instantly claimed due to the above cited Jindal et al. reference suggesting and motivating such species of ligand and separatory methods as described above. A well set forth specie in a generic disclosure of species is reasonably deemed to be therefore suggested and motivated therein which results in the practice of the above listed instant claims.

Claims 1-7, 17, 18, 21-23, 25, 58, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (P/N 6,358,692); taken in view of Hansson et al. (P/N 4,312,739).

The above rejection basis which is based on Jindal et al. is reiterated here. Jindal et al., suggests and motivates the practice of pH separation in column 4, lines 23-40, but lacks specifics of what is performed to accomplish this. The instant claims contain isoelectric focusing separation as an embodiment specie therein due to this being cited in instant claims 4 and 23.

Hansson et al. documents the old in the art technique of isoelectric focusing as a methodology for pH separation in the abstract. Protein sample isoelectric focusing is described in Hansson et al. in column 1, lines 6-20, and in column 7, Example I, directed to pH separation of proteins via such isoelectric focusing.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the methodology of Jindal et al. with suggestion and motivation to practice pH separation therein where details of such pH separation of proteins utilizing isoelectric focusing are set forth in Hansson et al. in order to accomplish the pH separation suggested and motivated in Jindal et al. to result in isoelectric focusing utilizing embodiments of the instant invention.

Claims 1-3, 5-8, 17, 18, 21, 22, 24, 25, 58, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (P/N 6,358,692); taken in view of Verentchikov et al. (P/N 6,545,268).

The above rejection basis which is based on Jindal et al. is reiterated here. Jindal et al., suggests and motivates the practice of mass spectrometry separation in column 4, line 17, but lacks specifics of ESI or TOF mass spectrometry as required in embodiments defined by instant claims 8 and 24.

Verentchikov et al. documents a variety of options within the practice of mass spectrometry separation and analysis. Protein sample mass spectrometry is described in Verentchikov et al. et al. in column 1, lines 32-36. A typical type of mass spectrometry is described as ESI or TOF mass spectrometry in column 2, lines 26-57, for such practice.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the methodology of Jindal et al. with suggestion and motivation to practice mass spectrometry separation and analysis therein where details of such mass spectrometry separation of proteins utilizing specifically ESI or TOF mass spectrometry as in instant claim 8 are set forth in Verentchikov et al. in order to accomplish such mass spectrometry separation and analysis suggested and motivated in Jindal et al. to result in instant claim 8 embodiments of the instant invention.

CLAIM OBJECTIONS

Claims 19, 20, and 71 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 33, 35, 39, 48, 50, 73-77, 80-82, and 91 are allowable.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., AU 1631 Supervisory Patent Examiner, whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 23, 2005

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER 1/23/05